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PRELIMINARY ASSESSMENT OF RELATIVE TOXICITY OF ETHYL CENTRALITE--ETC(U)
JUL 77 M H WEEKS, A H MCCREESH

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PRELIMINARY ASSESSMENT OF RELATIVE
TOXICITY OF ETHYL CENTRALITE
(N,N'-DIETHYLCARBANILIDE)
STUDY NO. 51-0923-77
APRIL 1976 - APRIL 1977

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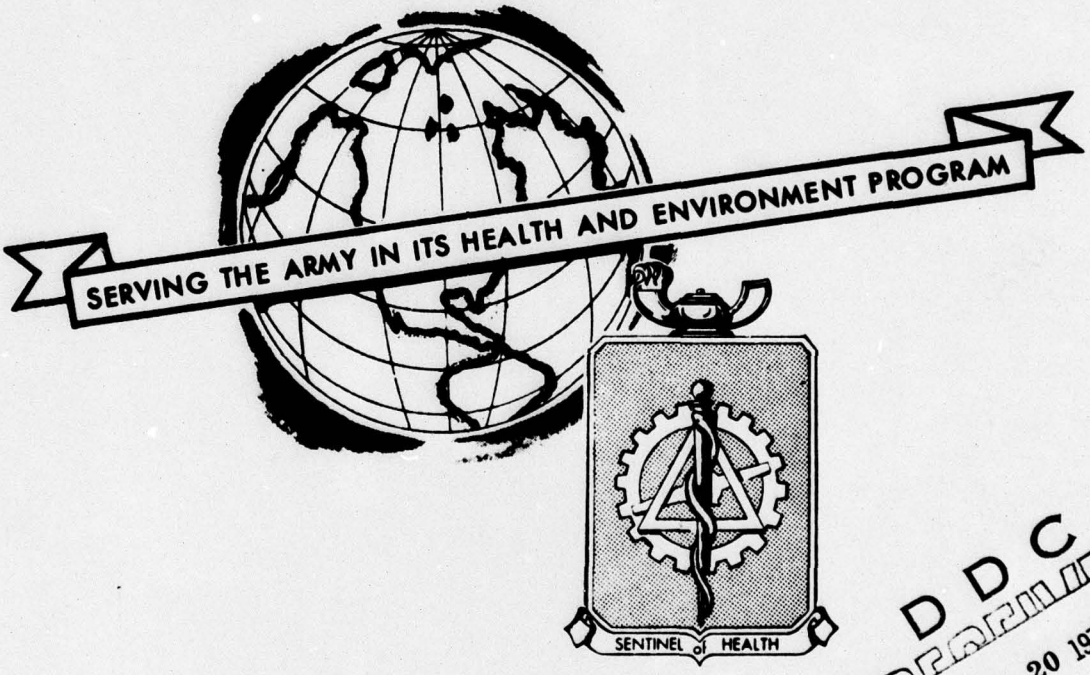

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skin irritation
eye irritation
sensitization studies
Centralite-1
acute inhalation vapor exposures
mutagenicity plate assay

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)
A hazard evaluation of ethyl centralite was performed using rats, rabbits and guinea pigs. Acetone solutions of the technical grade compound produced mild irritation when applied to the intact or abraded skin of rabbits, but the dry material did not. Direct application to rabbit eyes resulted in mild conjunctival irritation. Data indicated little toxic hazard from accidental ingestion or acute vapor inhalation. In vitro mutagenic studies were negative. It was recommended that personnel handling solid ethyl centralite wear approved eye and skin protective equipment.

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT/WP

15 JUL 1977

PRELIMINARY ASSESSMENT OF RELATIVE TOXICITY OF ETHYL CENTRALITE (N,N'-DIETHYLCARBANILIDE)

STUDY NO. 51-0923-77
APRIL 1976 - APRIL 1977

ABSTRACT

A hazard evaluation of the chemical ethyl centralite [N,N'-diethyl-N,N'-diphenylurea, Centralite-1] was performed by means of laboratory animal studies using rabbits, rats, and guinea pigs. The acetone solutions of the technical grade compound produced mild irritation when applied to the intact or abraded skin of rabbits, but the dry flake material did not. Mild injury to the conjuctiva resulted from a single application to the eyes of rabbits. Data indicated little toxic hazard from accidental ingestion. Acute vapor inhalation exposures of rats resulted experimentally in no deleterious effect. In vitro mutagenic studies were negative. It is recommended that personnel handling solid ethyl centralite should wear eye protection equipment in accordance with guidance provided in Title 29, Code of Federal Regulations, Part 1910.133. Personnel handling acetone solutions of this compound should wear skin protective equipment.

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT/WP

PRELIMINARY ASSESSMENT OF RELATIVE TOXICITY OF ETHYL CENTRALITE (N,N'-DIETHYLCARBANILIDE)

STUDY NO. 51-0923-77
APRIL 1976 - APRIL 1977*†

1. AUTHORITY. Letter, SARPA-S, Picatinny Arsenal, 15 April 1976, subject: Request for Toxicological Study of Ethyl Centralite, with indorsements thereto.

2. REFERENCE.

a. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972.

b. Title 29, Code of Federal Regulations, (CFR), 1976 ed., Part 1910, Occupational Safety and Health Standards.

c. Title 40, CFR, 1976 ed., Part 162, Regulations for the Enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act.

3. PURPOSE. The purpose of this study was to acquire information concerning the toxicity of ethyl centralite, by review of available data and by experimental studies in animals. This information provides a basis for advising on possible hazards associated with the handling of this compound in the preparation of propellants.

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 74-23, revised 1972, second printing 1974.
† The experiments reported herein were performed in animal facilities, fully accredited by the American Association for Accreditation of Laboratory Animal Care.

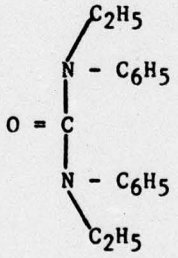
4. SUMMARY OF FINDINGS.

a. A literature search using the data base of the National Library of Medicine revealed no mammalian toxicological data pertaining to ethyl centralite. Sax[1] states that it is probably toxic but details are not known, and no backup literature is cited. He gives the explosion hazard as severe, as when shocked or exposed to heat. The disaster hazard is listed as being highly dangerous, shock and heat will explode it; when heated to decomposition, it emits highly toxic fumes. The Registry of Toxic Effects of Chemical Substances, page 299 (1976), gives only a mouse intraperitoneal LD_{50} of 200 mg/kg‡. A hazard evaluation of the material was conducted by this Agency using Sprague-Dawley, Wistar derived rats, New Zealand White rabbits, and Hartley guinea pigs. A summary of the properties of ethyl centralite follows:

ETHYL CENTRALITE

Diphenyl Diethylurea[2]
(Centralite I) (Mollite)

Composition: $[C_6H_5(C_2H_5)N]_2CO$



Properties: Almost colorless solid M.P. 79°C. Soluble in alcohol and ether. Readily converted to nitro derivatives by means of oxides of nitrogen.

Uses: As a stabilizer and as a deterrent for smokeless powder; to facilitate the gelatinization of collodion cotton with nitroglycerine.

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‡ National Technical Information Service, US Department of Commerce, Springfield, VA, AD 277-689

[1] Dangerous Properties of Industrial Materials, N. Irving Sax, 4th ed., Van Nostrand Reinhold Company, New York, pp. 642, 1975.

[2] Manual of Explosive Military Pyrotechnics and Chemical Warfare Agents, Jules Beibie, The MacMillian Company, New York, pp. 64, 1943.

b. Ethyl centralite (chemically, symmetrical diethyldiphenylurea, N,N'-diethyl-N,N'-diphenylurea, N,N'-diethylcarbanilide, CAS Number 000085983) is used as a non-volatile gelatinizer-stabilizer in smokeless propellants, serving also as a flash reducer (ref para 1). It has been proposed for use as an aging retardant in vulcanized rubber.[3] It has a gram molecular weight of 268.35, a melting point of 79°C, a boiling point of 326°C, is relatively non-volatile and insoluble in water. The sample used in these studies was received from Headquarters, Picatinny Arsenal, Dover, New Jersey, identified as coming from Lot 1123, as a pulverized white powder, conforming to Class 3 flaked (MIL-E-255A, Ethyl Centralite-carbamite).

c. Definitions of selected terms and abbreviations used in this report are found in Appendix A. Numerical data presented in the Appendices are expressed as the mean plus or minus one standard deviation. Statistical significance in this report has been selected at the .01 level of probability. A tabular presentation of animal toxicity data developed in this Agency follows:

[3] The Merck Index, Ninth Edition, Merck & Co., Inc., Rahway, N.J., p. 412, 1976.

Study No. 51-0923-77, Apr 76-Apr 77

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits. 0.5 g technical grade dry compound applied to each of six rabbits.	No primary irritation of the intact or abraded skin at 24 and 72 hours. Results are shown in detail in Appendix D.	Irritation category IV (reference Appendix B)
0.5 g technical grade compound in 1 ml acetone applied to each of rabbits.	Mild irritation and evidence of intact and abraded skin at 24 and 72 hours. No irritation at 7 days. Individual scores ranged from 0 to 2 with a mode of 1 (scoring see Appendix C). Results are shown in detail in Appendix E	
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 g technical grade dry compound to one eye of each of six New Zealand White rabbits.	No opacity noted in the eyes of rabbits at the 24-hour observation. Five of the six rabbits showed some conjunctival redness, chemosis and discharge. The eyes appeared normal after 72 hours. Results are shown in detail in Appendix F.	Irritation category III (reference Appendix B) Working with this compound may result in moderate eye irritation.

Study No. 51-0923-77, Apr 76-Apr 77

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
LD_{50}		
ORAL		
Rats		
Male (corn oil diluent)	LD_{50} - 2560 mg/kg (95% C.L. 1810 - 3160 mg/kg) Slope 3.41 ± 1.15; tremors, lethargy, tonic convulsions were seen at lethal dosages. Gross autopsy showed no tissue changes in decedents or survivors and no gross compound related changes were seen at 14-day necropsy. Details in Appendix G.	Toxicity category III (reference Appendix B)
SENSITIZATION STUDIES		
Guinea Pigs (Male)		
Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of ethyl centralite or of a 0.1 percent suspension of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of normal saline.		
Ten test guinea pigs received and were challenged with a 0.1 percent suspension of ethyl centralite	Challenge dose of ethyl centralite (last intradermal injection) produced no greater response than did the initial injection.	Test compound did not sensitize guinea pigs and is not expected to cause a sensitization reaction in humans.
Ten positive control guinea pigs received and were challenged with a 0.1 percent suspension of DNCB.	Positive control (DNCB) produced sensitization in 9 of 10 guinea pigs.	

* A known skin sensitizer.

Study No. 51-0923-77, Apr 76-Apr 77

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SENSITIZATION STUDIES		
Guinea Pigs (Male)		
Ten cage control guinea pigs: Five receiving challenge dose of ethyl centralite at 0.1 percent without prior sensitizing doses; five receiving challenge dose of DNCB at 0.1 percent without prior sensitizing doses.	Challenge dose of ethyl centralite and DNCB produced no greater response than did the initial injection in the test groups.	

Study No. 51-0923-77, Apr 76-Apr 77

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
ACUTE INHALATION VAPOR EXPOSURES		
Single 8-Hour Exposure		
Rats		
A group of six male rats was exposed to vapors of ethyl centralite at a nominal concentration of 0.4 mg/l. Dispersion tube held at 50°C; chamber flow 1 l/min.	Rats exposed to a nominal concentration of 0.4 mg/l for 8 hours showed no toxic signs during exposures and for 14 days thereafter. Body weight gain and organ-to-body weight ratios of the exposed rats compared to the control rats were not significantly different (reference Appendix I). No exposure related histopathologic changes were noted in tissues and organs.†	Compound has a low volatility and should present no acute inhalation hazard from single short term exposure.
A control group of six male rats was exposed to chamber air only at room temperature (23°C).		
A group of six male rats was exposed to vapors of ethyl centralite at a nominal concentration of 0 mg/l. Dispersion tube held at 23°C, chamber flow 1 l/min	No discernable loss of test material from dispersion tube was found. Rats showed no toxic signs during exposure and for 14 days thereafter. Body weight gain and the organ-to-body weight ratios of liver, kidney, lung, spleen and testes from exposed rats compared to the control rats were not significantly different (reference Appendix J). No exposure related histopathologic changes were noted in tissues and organs.	Compound has a low volatility and should present no hazard at room temperature due to the inhalation of ethyl centralite vapors.

† The following tissues and organs were examined: nasal turbinates, lung, heart, liver, spleen, esophagus, stomach, small and large intestine, kidney and testes.

Study No. 51-0923-77, Apr 76-Apr 77

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
ACUTE INHALATION VAPOR EXPOSURES		
Single 8-Hour Exposures		
Rats		
A group of six male rats was exposed vapors of ethyl centralite at a nominal concentration of 198 mg/l. Dispersion tube held at 100°C; chamber flow at 1 l/min.	Compound melted and vaporized from dispersion tube into exposure chamber; all compound had been dispersed in 80 minutes. Rats were thus only exposed for 80 minutes at a concentration of 198 mg/l. Rats showed no toxic signs during exposure and for 14 days therafter. Body weight gain and organ-to-body weight ratios of the exposed rats compared to the control rats were not significantly different (reference Appendix J).	Vapor presents no acute inhalation hazard from single short term exposure.
A control group of six male rats was exposed to chamber air only at room temperature (23°C).	No exposure related histopathologic changes were noted in tissues and organs.†	

† The following tissues and organs were examined: nasal turbinates, lung, heart, liver, spleen, esophagus, stomach, small and large intestine, kidney and testes.

Study No. 51-0923-77, Apr 76-Apr 77

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
MUTAGENICITY PLATE ASSAY ‡ (In Vitro Mutagenic Evaluation) A study was performed to evaluate ethyl centralite for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. One yeast strain, Saccharomyces cerevisiae, strain D4, and five bacteria strains of Salmonella typhimurium (TA-1535, TA-1537, TA-1538, TA-98, TA-100) were used in evaluating mutagenic potential. The compound was tested directly and in the presence of liver microsomal enzyme preparations from rats pretreated with Aroclor®. The compound was tested over a series of concentrations such that there was either quantitative evidence of same chemically-induced physiological effects at the high dose level. The low dose in all cases was below a concentration that demonstrated any toxic effect. The doses employed for the evaluation of this compound were 0.5µg, 5.0µg, 50µg, and 250µg per plate.	Nonactivation Tests Tests conducted on ethyl centralite in the absence of a metabolic system were all negative. Activation Tests Tests conducted on ethyl centralite in the presence of the rat liver activation system were all negative.	Ethyl centralite did not demonstrate mutagenic activity in any of the assays conducted in this evaluation and is considered not mutagenic under these test conditions.

‡ Work performed under contract by Litton Bionetics, Inc., Kensington, MD (LBI Project No. 2547, June 22, 1976).

® Aroclor is a registered trademark of Monsanto Chemical Co., 800 N. Lindberg Blvd, St. Louis, MO. Use of trade names does not imply endorsement by the US Army, but is used only to assist in identification of a specific product.

5. DISCUSSION. The low degree of hazard from inhalation of the vapor of ethyl centralite is partly due to its inability to vaporize in detectable concentrations at room temperature. Increasing the severity of the exposure by volatilizing the compound at 50°C and 100°C results in little apparent deleterious effect and further indicates that little hazard is expected from inhalation when handling this compound. The relatively low acute toxic hazard owing to ingestion coupled with the low potential for skin irritation indicate little hazard from handling the material except for its potential to produce mild conjunctival irritation. Personnel formulating and handling the compound represent the population at greatest risk and should wear eye protective equipment. It is unlikely that ethyl centralite presents a hazard as a potential high risk mutagen. The information given by Sax concerning the high risk hazard of ethyl centralite could not be verified in these studies and these warnings may be entirely unjustified.

6. CONCLUSION. The results of this study indicate that ethyl centralite should not present an occupational hazard to personnel in normal handling of this material.

7. RECOMMENDATIONS. It is recommended that personnel handling solid ethyl centralite should wear eye protective equipment, in accordance with guidance provided in 29 CFR 1910.133. Personnel handling acetone solutions of this compound should wear skin protective equipment.

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APPROVED:

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Director, Laboratory Services

APPENDIX A

GLOSSARY OF RECURRING DEFINITIONS, ABBREVIATIONS AND SYMBOLS USED BY THE TOXICOLOGY DIVISION, USAEHA

Definitions of medical terms and abbreviations used in this report are in agreement with the New Gould Medical Dictionary, Second Edition, published by the Blakiston Division of McGraw-Hill Book Company, Inc. Statistical terms and abbreviations are in agreement with those found in J. Maxwell Little's, An Introduction to the Experimental Method, 1961, Burgess Publishing Company, Minneapolis, MI. The following terms and abbreviations are either not found in the above references or have been modified to fit the special purposes of this report. Some of the terms have been included below for special emphasis.

WORD	DEFINITION
Acute Exposure	One exposure to exogenous test material for no longer than 8 hours. Animals are normally observed for 14 days after exposure.
Approximate Lethal Dose	In range finding the first dose of the lowest series of three ascending doses (each being 50 percent higher in concentration than the previous) all of which produce fatalities.
Hazard Evaluation	A study performed to estimate the degree of danger associated with the use of a material under specified conditions of use.
Nominal Concentration	Concentration of compound in the exposure chambers as determined by ascertaining the weight of the sample lost from the dispersion apparatus divided by total volume of chamber air used throughout the exposure time.
Primary Irritation	A local inflammatory reaction of the skin, produced by a compound, which does not produce destruction or irreversible change at the site of contact.
Subchronic Exposure	Repeated daily or constant exposure to a test material for no longer than 179 days or less than 2 days. Post observation period will vary.

Technical Grade Compound	As produced by the manufacturers of their commercial compound; definition dependent upon manufacturers' criteria.

Symbol	Meaning
>	is greater than
<	is less than
l/min	liters per minute
mg/l	milligrams of compound per liter of air
g	gram

APPENDIX B

TOXICITY CATEGORIES: 40 CFR 162

Hazard Indicators	I	II	III	IV
Oral LD_{50}	Up to and including 50 mg/kg	From 50 through 500	From 500 through 5,000	Greater than 5,000
Inhalation LC_{50} :				
(a) Dust or mist	Up to and including 2.0 mg/l	From 2.0 through 20	From 20 through 200	Greater than 200
(b) Gas or vapor	Up to and including 200 p/m	From 200 through 2,000	From 2,000 through 20,000	Greater than 20,000
Dermal LD_{50}	Up to and including 200 mg/kg	From 200 through 2,000	From 2,000 through 20,000	Greater than 20,000
Eye effects	Irreversible corneal opacity at 7 days	Corneal opacity reversible within 7 days or irritation persisting for 7 days	No corneal opacity irritation reversible within 7 days	No irritation
Skin irritation	Severe irritation or damage at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours	No irritation at 72 hours

APPENDIX C

EVALUATION OF SKIN REACTIONS

Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness to slight eschar formation)	4

Edema Formation

No edema	0
Very slight (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

An individual irritation score is equal to the sum of the scores for edema formation and erythema and eschar formations.

APPENDIX D

COMPOUND: Ethyl Centralite								USAEHA STUDY NO. 51-0923-77	
PRIMARY SKIN EFFECTS NEW ZEALAND WHITE RABBITS .		IRRITATION CATEGORY* IV						CONDITIONS - Dry Powder Ethyl Centralite - Single 24-hour application of 0.5 g dry white crystalline powder per skin application site	
	Time of Observation	Response Rabbit No.							
	Hours	1	2	3	4	5	6	Mean Score	Comments
Erythema & Eschar									
Intact Skin	24	0		0		1		0.33	
Intact Skin	72	0		0		0		0.00	
Abraded Skin	24		1		0		0	0.33	
Abraded Skin	72		0		0		0	0.00	
						Subtotal		0.66	
Edema Formation									
Intact Skin	24	0		0		0		0.00	
Intact Skin	72	0		0		0		0.00	
Abraded Skin	24		0		0		0	0.00	
Abraded Skin	72		0		0		0	0.00	
						Subtotal		0.00	
						Total		0.66	

* 40 CFR 162, Lot No. 1123

APPENDIX E

COMPOUND: Ethyl Centralite								USAEHA STUDY NO. 51-0923-77
PRIMARY SKIN EFFECTS NEW ZEALAND WHITE RABBITS		IRRITATION CATEGORY* III						CONDITIONS - Acetone solution Ethyl Centralite - Single 24-hour application of 0.5 g compound in 1.0 ml acetone per skin application site
	Time of Observation	Response Rabbit No.						
	Hours	1	2	3	4	5	6	Mean Score / Comments
Erythema & Eschar								
Intact Skin	24		0		1		0	0.33 — No irritation at 7 days after application.
Intact Skin	72		2		0		0	0.67
Abraded Skin	24	2		1		0		1.00
Abraded Skin	72	2		2		1		1.67
						Subtotal		3.67
Edema Formation								
Intact Skin	24		1		1		1	1.00
Intact Skin	72		1		0		0	0.33
Abraded Skin	24	1		1		1		1.00
Abraded Skin	72	2		2		1		1.67
						Subtotal		4.00
						Total		7.67

* 40 CFR 162, Lot No. 1123

APPENDIX F

COMPOUND: Ethyl Centralite								USAEHA STUDY NO. 51-0923-77	
ACUTE EYE EFFECTS NEW ZEALAND WHITE RABBITS		IRRITATION CATEGORY* III						CONDITIONS - Unwashed Eye Test Ethyl Centralite - Single 24-hour application of 0.1 g of dry white crystalline compound to one eye of each rabbit	
Time of Reading		Scores Rabbit No.							
Hrs-Days	Structure	1	2	3	4	5	6	Mean Score	Comments
24	Cornea	0	0	0	0	0	0	0.0	No corneal opacity. conjunctivae irritation reversible within 3 days
	Iris	0	0	0	0	5	0	0.8	
	Conjunctivae	0	4	12	2	16	2	6.0	
48	Cornea	0	0	0	0	0	0	0.0	
	Iris	0	0	0	0	0	0	0.0	
	Conjunctivae	0	0	6	0	6	0	2.0	
72	Cornea	0	0	0	0	0	0	0.0	
	Iris	0	0	0	0	0	0	0.0	
	Conjunctivae	0	0	0	0	0	0	0.0	
7-Days	Cornea	0	0	0	0	0	0	0.0	
	Iris	0	0	0	0	0	0	0.0	
	Conjunctivae	0	0	0	0	0	0	0.0	
* 40 CFR 162, Lot No. 1123									

The eye injury is evaluated according to a weighted scoring system used by Draize et.al. Draize, J.H., Woodward, G. and Calvary, H.O. Method for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes, J. Pharmacol and Exp Therap., 82: 377-390, 1944.

APPENDIX G

COMPOUND: Ethyl Centralite — USAEHA STUDY NO. 51-0923-77

ACUTE ORAL LD_{50}
MALE RATS
SPRAGUE-DAWLEY, WISTAR
TOXICITY CATEGORY - III

LD_{50}* 2560 mg/kg — 95% C.L. 1810-3160 mg/kg
Slope 3.41 — S.E. ±1.15
Conditions Diluent corn oil, 10 g ethyl centralite (dry crystalline powder) dissolved in 40 ml corn oil

Dosage	Conc	Onset of signs (s), mortality (m)										Mort	Mean Body Wt.		Mean Body Wts. (g)			
		Hours			Days							Cumula-			Days			
	%	0-4	4-12	12-24	2	3	4	5	6	7	8-14	tive	Init	Fin	1	3	7	14
1000	25											0/6	196 ±7	267 ±17	201 ±7	204 ±14	241 ±15	267 ±17
1260	25		M2									2/6	193 ±5	271 ±5	204 ±8	206 ±4	244 ±5	271 ±5
1590	25		M2									2/6	203 ±16	273 ±15	187 ±6	201 ±4	244 ±9	273 ±15
2000	25		M1									1/6	205 ±11	272 ±21	190 ±15	206 ±14	246 ±16	272 ±21
2510	25	M1	M1									2/6	203 ±15	255 ±17	183 ±23	188 ±30	231 ±23	255 ±17
3160	25	M2	M2									4/6	190 ±15	268 ±14	185 ±32	186 ±39	235 ±30	268 ±24
3980	25	S6	M5									5/6	184 ±2	163 -	165 -	211 -	245 -	163 -
Control	--											0/6	176 ±2	241 ±12	176 ±4	188 ±6	223 ±11	241 ±12

Signs of Intoxication: Tremors, lethargic, tonic convulsions at lethal dosages, wet anus, ruffled pelt, red discharge around eye.
Gross Autopsy: No changes in decedents or survivors. No gross compound related changes seen at necropsy (+14 days)

*Probit analysis by the method of Bliss. Bliss, C. I. (1952), The Statistics of Bioassay, Vol II Academic Press, New York.

Lot No. 1123

APPENDIX H

COMPOUND: Ethyl Centralite — USAEHA STUDY NO. 51-0923-77

GUINEA PIG SENSITIZATION
MALE
HARTLEY STRAIN

Substance: Ethyl Centralite

Identity: Intradermal injection-Ten sensitizing doses of 0.1 ml of a 0.10% solution in saline.
Positive Control - Dinitrochlorobenzene (DNCB)

24 Hrs	Mean Body Weight (g) Initial	Mean Body Weight (g) Final	Diluent Initial	Diluent Final	Test Compound Initial	Test Compound Final
Test Cmpd	316 ±23	494 ±43	0	0	0	3
Positive Control	325 ±42	517 ±41	0	0	37	262

48 Hrs	Mean Body Weight (g) Initial	Mean Body Weight (g) Final	Diluent Initial	Diluent Final	Test Compound Initial	Test Compound Final
Test Cmpd			0	0	0	0
Positive Control			0	0	4	285

Comments

Test compound did not produce a sensitization reaction in guinea pigs.

DNCB positive control showed a sensitizing reaction in 10/10 guinea pigs.

Final Scores

>100 - Strong Sensitizing
25 - 100 - Mild Sensitizing
<25 - No Sensitizing

H-1

Study No. 51-0923-77, Apr 76-Apr 77

APPENDIX I

ACUTE INHALATION EXPOSURE
SINGLE 8-HOUR EXPOSURE OF MALE RATS
TO VAPORS OF ETHYL CENTRALITE

TABLE 1. MEAN BODY WEIGHT (g).

Treatment Group	Pre-Exposure Day 0	Post Exposure Day 1	3	7	11
Chamber Control	147 ±16	149 ±16	159 ±18	182 ±21	233 ±29
Exposure at 23°C	153 ±9	157 ±11	167 ±10	190 ±11	244 ±15
Exposure at 100°C	154 ±4	157 ±5	173 ±4	195 ±6	256 ±6

TABLE 2. ORGAN-TO-BODY WEIGHT RATIOS OF MALE RATS NECROPSIED 14 DAYS AFTER EXPOSURE

Treatment Group	Mean Terminal Body Weight g	Mean Organ-to-Body Weight Ratios Grams Per 100 Grams Body Weight Liver	Kidney	Spleen	Lung	Testes
Chamber Control	233 ±29	4.46 ±.29	.83 ±.05	.32 ±.07	.58 ±.10	1.05 ±.05
Exposure at 23°C	244 ±15	4.57 ±.07	.81 ±.04	.36 ±.03	.57 ±.05	1.04 ±.07
Exposure at 100°C	256 ±6	4.75 ±.15	.82 ±.07	.42 ±.05	.61 ±.07	1.04 ±.07

APPENDIX J

ACUTE INHALATION EXPOSURE
SINGLE 8-HOUR EXPOSURE OF MALE RATS
TO VAPORS

TABLE 1. MEAN BODY WEIGHT (g).

Treatment Group	Pre-Exposure Day 0	Post Exposure Day 1	Post Exposure Day 3	Post Exposure Day 7	Post Exposure Day 14
Chamber Control	191 ±26	193 ±25	199 ±23	220 ±28	292 ±35
Exposure at 50°C	185 ±12	186 ±12	192 ±12	216 ±13	274 ±10

TABLE 2. ORGAN-TO-BODY WEIGHT RATIOS OF MALE RATS NECROPSIED 14 DAYS AFTER EXPSOURE.

Treatment Group	Mean Terminal Body Weight g	Mean Organ-To-Body Weight Ratios Grams Per 100 Grams Body Weight Liver	Kidney	Spleen	Lung	Testes
Chamber Control	292 ±35	4.10 ±.25	.75 ±.11	.31 ±.04	.56 ±.05	.97 ±.14
Exposure at 50°C	274 ±10	4.30 ±.15	.79 ±.03	.31 ±.03	.61 ±.04	1.04 ±.06